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Portable optical microscope-on-a-chip

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ABSTRACT

In this paper, we present a novel high resolution optical imaging device on chip. It is based on a line of nano holes defined in an optically opaque aluminum film on a CMOS imaging sensor chip. Because it's free of bulky optical elements and compatible to the planar micro fabrication process, it is very promising to become an important component for the on-chip high resolution imaging in the future. The fabrication and operation of this novel on-chip microscope is explained in details. The performance is evaluated theoretically and is verified experimentally by examining the profile of a laser spot formed by a 10X objective lens.

Keywords: Optofluidics, Biophotonics, Nanophotonics, Microfluidics, Microscopy, Beam profiler.

1. Introduction

The advantages of compactness and cost effectiveness of micro total analysis system (μTAS) have made μTAS very attractive in making portable and point-of-care instruments for the life sciences and clinical practice[1,2]. In recent years, many achievements have been made in the fields, such as fluidic transportation, sample manipulation, chemical sensing, and sample sorting. But the on-chip high resolution (~1μm or better) imaging need has not been satisfactorily addressed. The high resolution imaging in existing microfluidic systems is fulfilled by using bulky conventional microscopes[3,4] at present, which obviates the cost and size advantages of micro analysis systems.

Our group proposed a novel on-chip imaging technique that can be directly integrated into a microfluidic network, and can therefore enable on-chip imaging in a microfluidic system. It is termed Optofluidic Microscopy (OFM). In this paper, we present, to our knowledge, the first high resolution on-chip imaging device. The performance is evaluated theoretically and is verified experimentally by examining the profile of a laser spot formed by a 10X objective lens.

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2. Method

The on-chip OFM system is fabricated on a MT9V403 CMOS imaging sensor from Micron Technology, Inc. The pixel size is 9.9μm x 9.9μm. A 100nm thick aluminum thin film is coated onto the CMOS sensor by thermal evaporation as an optically opaque mask for the CMOS pixels. Then a FEI dual beam focus ion beam machine is used to mill nano holes through the aluminum film at the centers of a line of CMOS pixels. The through holes are 500nm in diameter, as shown in Figure 1. The nano through holes on the aluminum film acting as nano apertures confine the light sampled by the pixels of CMOS imaging sensor. The diameter of the nano apertures determines the fundamental resolution limit of OFM.

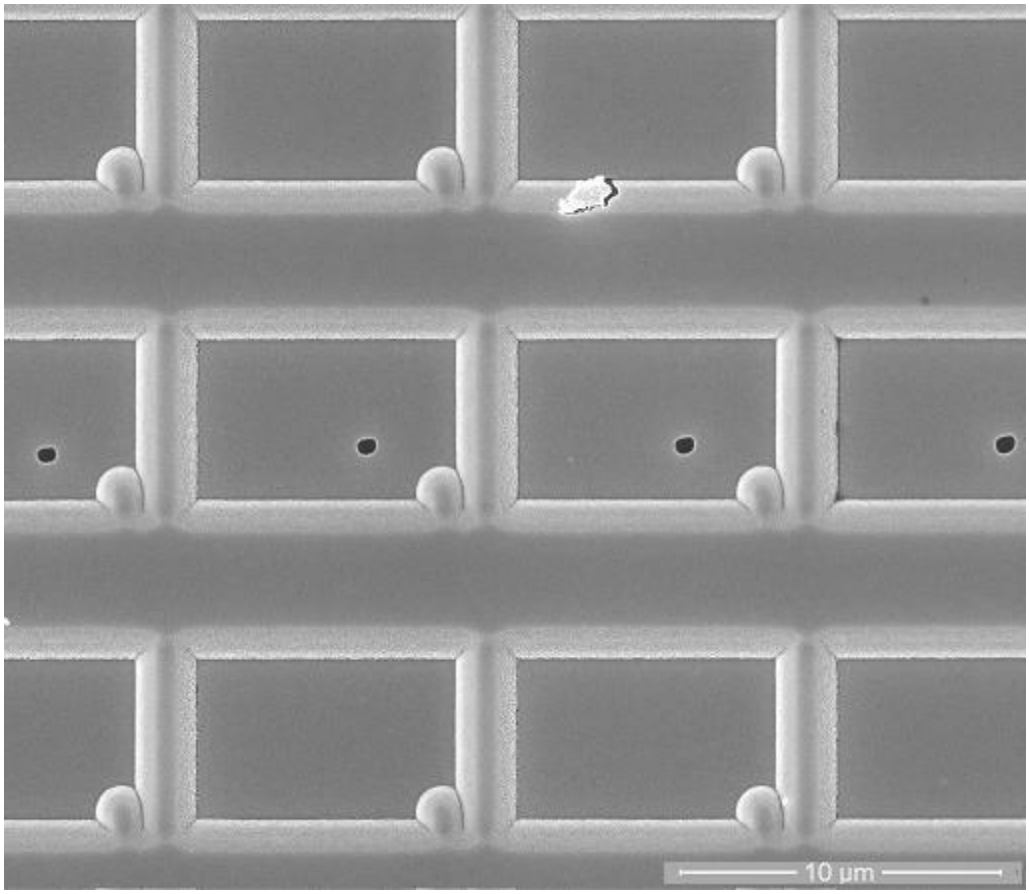


Figure 1: 500nm apertures milled on the aluminum film at the centers of a line of CMOS pixels by the focus ion beam machine.

Figure 2 provides an overview of the operating principle of the OFM. A target light field is scanned on the CMOS imaging sensor in a slightly different direction with respect to the line of nano apertures at a constant scanning speed v. The angle between the scanning direction and the line of nano apertures is called scanning angle θ. When the light field is scanned over a nano aperture on top of a CMOS pixel, only the portion of light above the nano aperture will be sampled by the CMOS pixel underneath. So the CMOS pixel will record a line profile of the portion of the light field crossing it during the scanning. The same thing will happen to the other CMOS pixels, when the target light field scanning across them. Because of the periodic distribution of the nano apertures, the target light field will be 'sliced' uniformly by the nano apertures. And the 'sliced' line profiles will be recorded by the corresponding CMOS pixels. Because of the spacing between adjacent nano apertures, there is a time delay in the sampling time of the target light field between adjacent CMOS pixels. The time delay is equal to the time that the target light field travels across two adjacent nano apertures in the scanning direction. It is a constant for a constant scanning speed v. By knowing the sampling time delay between the line profile signals recorded by adjacent CMOS pixels, the signals sampled by different pixels can be reconstructed to form a complete profile of the target light field.

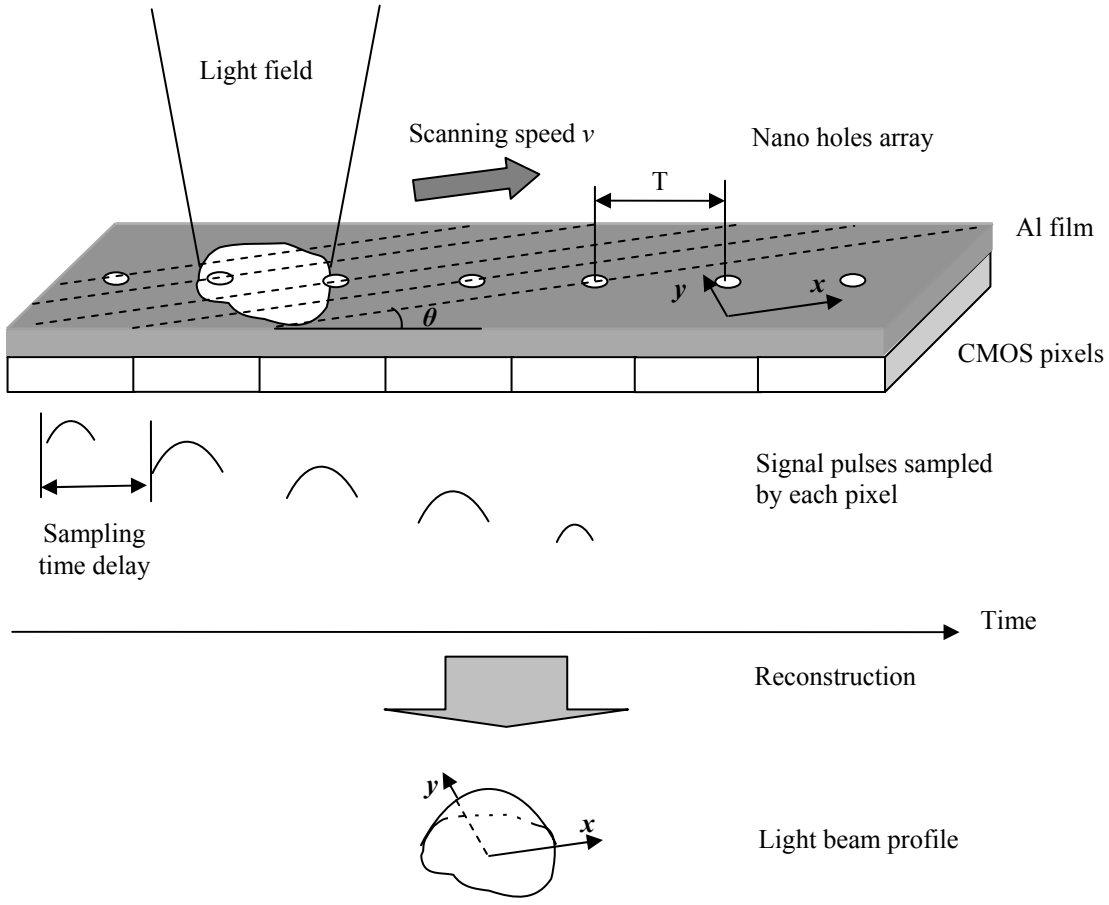


Figure 2: Operating principle of the OFM.

3. Theoretical analysis

Since on-chip OFM is a novel imaging system, the theoretical study of the performance is necessary. For clearance, we define the scanning direction as *x*, and the direction perpendicular to it as *y*. The resolution of on-chip OFM system in *y* direction, which is perpendicular to the scanning direction, is determined by the spacing between adjacent nano apertures in the *y* direction.

$$R_y = T \sin\theta \tag{3.1}$$

where *T* is the pitch of nano apertures, and θ is the angle between the scanning direction *x* and the line of nano apertures. According to the Eq. (3.1), the resolution of on-chip OFM system in *y* direction can be increased by either decreasing the pitch of nano apertures or by decreasing the scanning angle. The former is not practical, since usually the pitch of nano apertures is a constant for a certain CMOS sensor in use. The latter can be realized all the time in theory. But the resolution of on-chip OFM system in *y* direction can't be better than the diameter of individual nano aperture, since it's the smallest sample unit in OFM.

The resolution of on-chip OFM system in *x* direction, the scanning direction, is determined by the traveled distance of the light field between two sequent sampling times.

$$R_x = \frac{v}{fps} \tag{3.2}$$

where *v* is the scanning speed, and *fps* is the frame rate of the CMOS sensor. According to the Eq. (3.2), the resolution of on-chip OFM system in *x* direction can be increased by decreasing the scanning speed of the light field or by increasing the frame rate of CMOS sensor. The former is usually restricted by the capability of linear scanner or the lowest flow speed we can get if the OFM is used in microfluidic imaging. The later is limited by the illumination intensity in OFM imaging and capability of the CMOS sensor. But the resolution of on-chip OFM system in *x* direction can't be better than the diameter of individual nano aperture too, since it's the smallest sample unit in OFM.

If the noise of the CMOS sensor is considered, the ultimate resolution limit of the OFM system is determined not only by the size of individual nano aperture, but also by the illumination intensity and the transmission of nano apertures.

As described in Ref. 5, if the photon counting noise (shot noise) and the receiver noise ($n_r\tau$) are considered as the dominating noise sources, the sensitivity (SNR, or signal to noise ratio) of OFM can be expressed as:

$$SNR = \frac{N_T}{\sqrt{N_T + (n_r\tau)^2}} \tag{3.3}$$

where N_T : the total transmission photon count for a pixel dwell time τ (also equivalent to the inverse of frame rate). By considering the performance of OFM in both large hole and small hole limit, the possibility of creating OFM devices with resolution of sub 100 nanometers is predicted[5].

4. Experimental results

In order to test and verify the performance of the OFM system, we set up a beam profiler test bench for the OFM system, in Figure 3. A 632nm collimated laser beam is focused onto the OFM by a 10X objective lens from Newport. The OFM is mounted to a X-Y translation stage driven by two independent 850G actuators from Newport. Instead of scanning the focused laser beam on the OFM, the OFM is moved by the linear scanner controlled by one of the 850G actuator. The OFM is mounted in such a way that the angle between the scanning direction and the line of nano apertures is 9.5 degree.

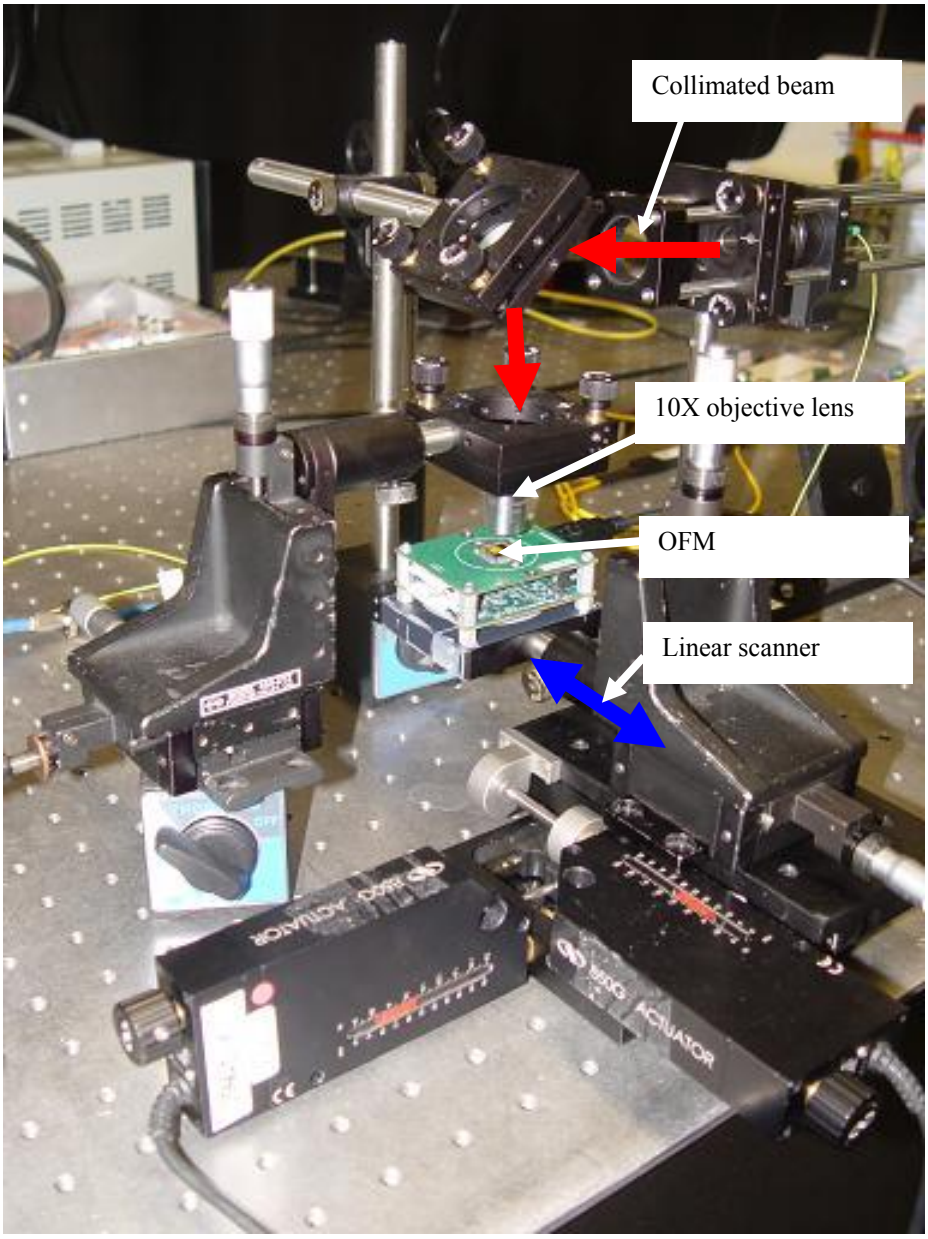


Figure 3: The beam profiler test bench for the OFM system

The exposure time of the CMOS sensor is set to 1.5ms. The frame rate of the CMOS sensor is 640Hz. When the OFM is scanned at the constant speed of 0.1mm/s, 4000 frames of raw data is recorded by 32 sequent nano apertures, which is shown in Figure 4 (a).

When the image is reconstructed according to the sampling time delay of adjacent CMOS pixels under the scanning speed of 0.1mm/s, the line profile signals sampled by each pixel join together again and form a reasonable pattern of the focused laser spot, Figure 4(b).

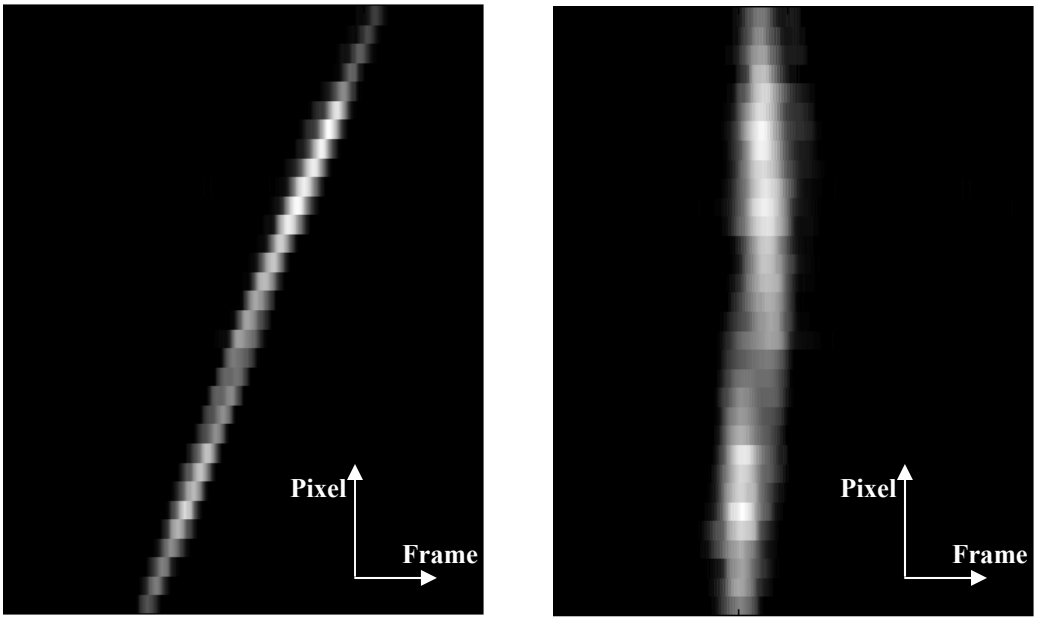
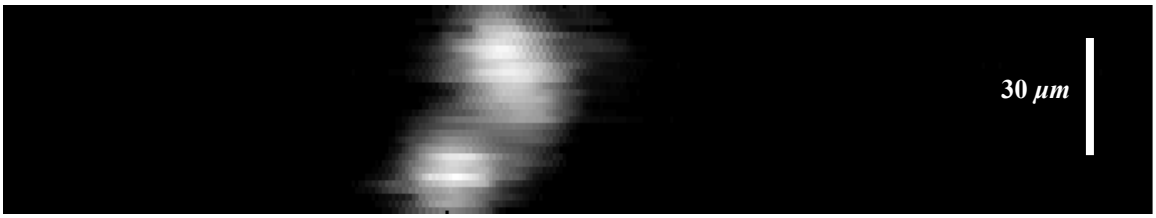


Figure 4: (a) 4000 frames of raw data recorded by 32 sequent nano apertures. (b) Reconstructed OFM image according to the scanning speed of 0.1mm/s.

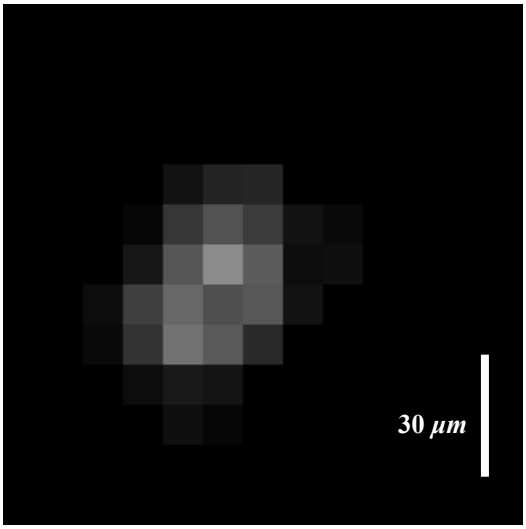
According to the frame rate, number of the frames, the actual horizontal dimension of the reconstructed image is 305μm. According to the pitch of the nano apertures and the scanning angle, the vertical dimension of the reconstructed image is 53 μm. Figure 5 (a) is the rescaled OFM image according to the actual aspect ratio. For comparison, without changing the focus, the focused laser spot is moved to the area of the same CMOS sensor without nano apertures, and the profile of the laser spot is recorded directly by the CMOS pixels right underneath it. Figure 5 (b) shows the 20 times magnified image of the focused laser spot taken directly by the same CMOS sensor under the same condition. The reconstructed OFM image in Figure 5 (a) is very similar to the one taken directly by CMOS sensor in Figure 5 (b), and they also have the similar dimension. It proves the credibility of the reconstructed OFM image. But on the other hand apparently we see more details in Figure 5 (a) than in Figure 5 (b). It shows the OFM indeed can achieve better resolution than the direct imaging by CMOS sensor.

The vertical resolution of this OFM image R_y in Figure 5 (a) is around 1.6 μm, which is larger than the size of individual nano aperture. The vertical discontinuity in Figure 4 (b) confirms the under-sampling in the vertical direction of the OFM image. It can be improved by decreasing the scanning angle. The horizontal smooth profile of this OFM image R_x shows sufficiently sampling in the horizontal direction. The actual

horizontal resolution of the OMF image is determined by the diameter of individual nano aperture and the noise of the CMOS sensor.



(a)



(b)

Figure 5: (a) The rescaled OFM image of the focused laser spot according to the actual aspect ratio. (b) The 20 times magnified image of the same focused laser spot taken directly by the same CMOS sensor under the same condition.

5. Conclusion and future work

The fabrication and the principle of the OFM systems are discussed in details. The performance of the OFM is studied in theory and verified in experiment. All of these have shown that the OFM is really a promising device for the high resolution on-chip imaging.

In the next step, we will integrate microfluidic and micro analysis systems on top of OFM to implement some fully functional biomedical or bioimaging systems. Figure 6 shows the idea of a fully automated and miniaturized live single or multiple cell organism analysis system. The organism can be feed or mixed with reagent in the chamber. The OFMs can be added into the circulation channels of the system to monitor the morphology change of the micro organism induced by growth or external stimuli.

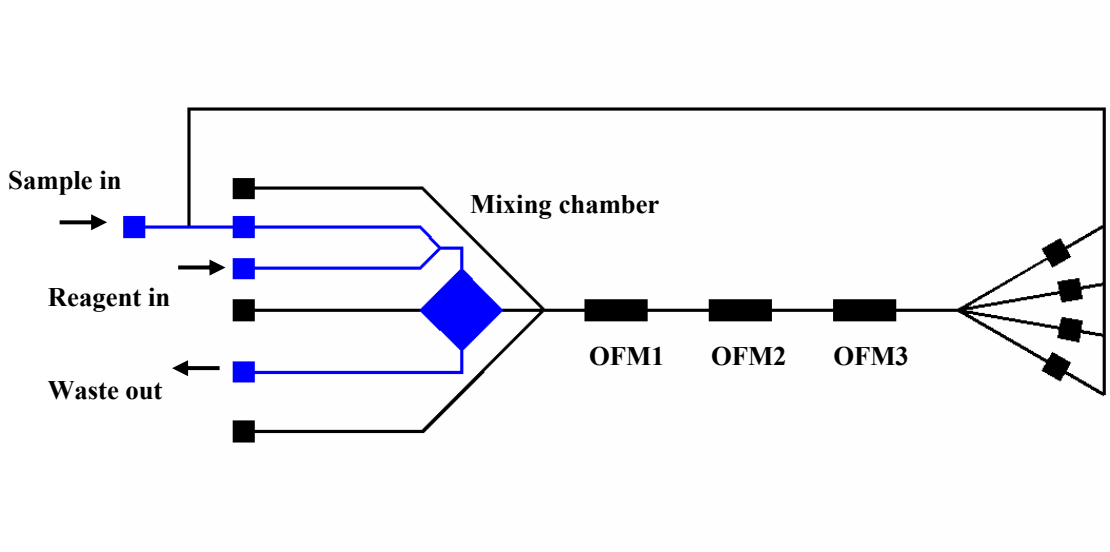


Figure 6: A fully automated and miniaturized live single or multiple cell organism analysis system.

6. Acknowledgement

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